REMARKS

Claims 1-25, 74 and 75 are pending in the application. Claims 26-73 are hereby canceled. Claims 74 and 75 are hereby added. Favorable reconsideration of the application is respectfully requested.

Election/Restriction

Claims 29-55 and 65-73 have been withdrawn as being directed to non-elected inventions and are hereby canceled without prejudice to further prosecution in a subsequent continuation or divisional application.

Claim Objections

Claims 26-28 and 56-64 are objected to. In order to simplify the issues in the present prosecution, these claims are hereby canceled without prejudice to further prosecution in a subsequent continuation or divisional application.

Claim Rejections under 35 U.S.C. §112

Claims 1-28 and 56-64 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for the recitation "the at least one component" in line 9. The claim has been amended to provide proper antecedent basis for this recitation.

Claim 25 is further rejected as vague and indefinite because the claim does not end in a period. The claim has been amended to provide the inadvertently omitted period.

Accordingly, withdrawal of the rejections under 35 U.S.C. §112 is respectfully requested.

Claim Rejections under 35 U.S.C. §§102 & 103

Claims 1-7, 26-28 and 56-64 were rejected under 35 U.S.C. §102 as anticipated by Zuckermann et al. (WO 98/42730) ("Zuckermann"). Claims 8-25 were rejected under 35 U.S.C. §103 as unpatentable over Zuckermann.

The presently claimed invention is directed to a method for providing a biological sample component expression pattern for a biological sample. The method involves applying a biological sample to an affinity support composed of one or more ligands coupled to a biological sample-compatible matrix. As noted in the Summary section of the application at page 5, lines 1-19, in particular lines 1-4, and in the Detailed Description section of the application at page 10, line 15 to page 11, line 12, in particular page 10, line 16 to page 11, line 5, the affinity support

materials of the present invention have intermediate and controllable binding affinity for biological samples, relative to conventional materials. According to this aspect of the invention, the components of the sample are fractionated on the affinity support to provide an enriched fraction, and a biological sample component expression pattern for the biological sample is determined using the enriched fraction.

"Intermediate and controllable binding affinity support materials" refers to materials capable of interacting with the constituents of a biological sample by a combination of ionic, van der Waal's, and hydrogen bond interactions akin to protein-protein, protein-oligonucleoside (oligonucleotide), or oligonucleoside (oligonucleotide)-oligonucleoside (oligonucleotide) interactions. In general, the supports and associated methods provided by the present invention combine the attributes of general resins typically based on one functional group (like anion or cation exchange resins) and highly specific affinity resins based on a particular combination of several functional groups chosen for a single, specific target constituent. Therefore, the supports will have an intermediate binding affinity that still yield high affinities in many cases, but will have a broader specificity than an affinity resin.

As noted by the Examiner, Zuckermann is directed to substrates that that have a surface that is hydrophilic in one state and hydrophobic in another state, so that the substrate can be used in either aqueous or organic media. The substrate surface contains a number of hydrophilic groups that may be protected during synthesis of ligands on the substrate in organic media, and then deprotected to regenerate the surface in hydrophilic form suitable for conducting, for example, screening and or separation procedures in aqueous media. The Examiner further notes that a plurality of chemically distinct ligands may be provided on the substrate, such that a ligand of interest may be identified by screening for said ligand.

Thus, while the Zuckermann reference may describe an inventive substrate and technique for functionalizing that substrate to conduct screening of biological samples, the reference does not address the character of the ligands with which the substrate is functionalized in any categorical way. As noted above, the present invention is directed to a novel category of affinity support materials and, in the presently pending claims, techniques for their use in determining biological sample component expression patterns. The ligands on the affinity support materials of the present invention are selected and configured to confer an intermediate level of binding affinity for biological sample components. Those of skill in the protein and nucleotide chemistry arts will appreciate that the support materials of the present invention differ significantly from the materials taught by the prior art for separating the components of biological samples, as the materials taught by the prior art use only very general and uncontrollable interactions with biological sample components (*e.g.*, charge-based) or very specific and controlled (*e.g.*,

antibody-based) binding affinities, but nothing intermediate these extremes. Claim 1 has been amended to clarify and emphasize this important aspect of the present invention.

While the Zuckermann reference identifies a variety of possible ligands for functionalization of the described substrates, there is no teaching that the ligands be selected and configured on the substrate to provide an intermediate level of binding affinity. Such selection and configuration of ligands is detailed in the application and in recited in dependent claims 4-20. Without teaching to this effect, Zuckermann must be appropriately read to teach the use of ligands in a conventional manner on the inventive substrate, that is, ligands configured to have very general and uncontrollable interactions with biological sample components (*e.g.*, charge-based) or very specific and controlled (*e.g.*, antibody-based) binding affinities. An intermediate binding affinity category is not addressed. Accordingly, since Zuckermann lacks any teaching or suggestion of this important feature of the claimed invention, it is respectfully submitted that claim 1, as amended, is patentable over the cited art. The remaining claims depend from claim 1 and are submitted to be patentable for at least the reasons noted for claim1. Thus, withdrawal of the rejections under §§102 and 103 is respectfully requested.

New Claims

Claims 74-77 are added to claim additional detail relating to certain aspects of the invention, namely, further characterization of the affinity support material ligands used and some specific affinity support material support ligands used.

Conclusion

Applicants believe that all pending claims are allowable and respectfully request a Notice of Allowance for this application from the Examiner. Should the Examiner believe that a telephone conference would expedite the prosecution of this application, the undersigned can be reached at the telephone number set out below. If any additional fees are due in connection with the filing of this amendment, the Commissioner is authorized to charge such fees to Deposit Account 500388 (Order No. CHIRP012).

Respectfully submitted,
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APPENDIX I

AMENDMENTS MADE TO CLAIMS

1. A method of determining a biological sample component expression pattern for a biological sample, comprising:

applying a biological sample to an affinity support comprising a ligand coupled to a biological sample-compatible hydrophilic matrix, said ligand comprising a backbone having a plurality of affinity property groups and hydrophilic groups pendent therefrom, and said ligand **having an intermediate binding affinity for components of the biological sample and** being configured to at least partially resolve **at least one** component**[s]** of a said biological sample;

resolving the at least one component of the biological sample to provide thereby an enriched fraction; and

determining a biological sample component expression pattern for the biological sample using the enriched fraction.

25. The method of claim 23, wherein said heterogeneous source is one or more blood samples.

26-73. (canceled)

The following claims are added:

74. The method of claim 1, wherein the intermediate binding affinity is characterized by the ligand interacting with the components of the biological sample by a combination of non-specific molecular forces consisting essentially of ionic, van der Waal's and hydrogen bond interactions.

75. The method of claim 4, wherein the ligand is selected from the group consisting of the following: